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D. Margaret Seaman, Examiner GAU 1625 Patent and Trademark Office	703/872-9306	

**FROM:** Martha A. Robinson**USER ID:** MR10031 **FLOOR:** 20**PHONE:** (512) 536-5616**FAX:** (512) 536-4598**RE:** RESUBMISSION OF IDS AND FORM PTO-1449**NUMBER OF PAGES WITH COVER PAGE:** 16 **Originals Will Not Follow****Message:**

U.S. Application No. 09/506,988 entitled "PROTEASE INHIBITORS THAT OVERCOME DRUG RESISTANCE" by Tang and Ghosh.

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Date

Steven L. Highlander

D. Margaret Seaman, Examiner  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 09/506,988 entitled "PROTEASE INHIBITORS THAT  
OVERCOME DRUG RESISTANCE" — Jordan J.N. Tung and Arun K. Ghosh*  
*Our reference: OMRP:056US*  
*Client reference:*

Dear Examiner Seaman:

After reviewing each of the Office Actions and the Notice of Allowability, it has come to our attention that the Information Disclosure Statement, Form PTO-1449 and 57 references submitted on July 25, 2000, were apparently never signed off by an Examiner.

For your convenience we have enclosed a copy of a Supplemental Information Disclosure Statement and Form PTO-1449 that was filed with the Patent and Trademark Office (PTO) on July 25, 2000. Also enclosed is a copy of PTO stamped postcard indicating the documents submitted. The copies of the references previously submitted have not been enclosed. Please let us know if you would like us to resubmit those as well.

Please review and approve this Supplemental Information Disclosure Statement. If you need additional information, please let us know.

Thank you for your assistance in this matter.

Respectfully submitted,

Steven L. Highlander  
Reg. No. 37,642

SLH/mar  
Encl: as noted  
35529204.1

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The "Received" stamp of the Patent Office imprinted hereon acknowledges the filing of:

Applicant(s): Jordan I.N. Tang and Anun K. Ghosh

Serial & Docket Nos.: 09/506,988 OMRF 176

Filed: February 18, 2000

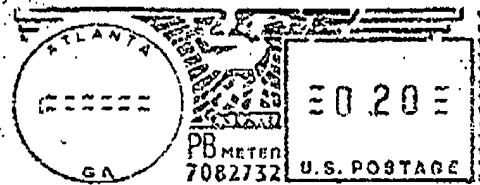
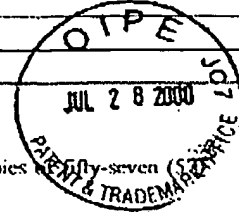
Papers Submitted:

Information Disclosure Statement, six (6) pages of Form PTO-1449, and copies of fifty-seven (57) documents cited therein.

Date: July 25, 2000

Client/Matter No.: 20487/244

By: Patrea L. Pabst, Reg. No. 31,284



Patrea L. Pabst, Esq.  
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Applicants: Jordan J.N. Tang and Arun K. Ghosh

Serial No.: 09/506,988

Art Unit:

Filed: February 18, 2000

Examiner: Not Yet Assigned

For: *PROTEASE INHIBITORS THAT OVERCOME DRUG RESISTANCE*Assistant Commissioner for Patents  
Washington, D.C. 20231**INFORMATION DISCLOSURE STATEMENT**

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including six (6) pages of Form PTO-1449 and a copy of each document cited therein.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 01-2507.

**Publications**

BALDWIN, et al., "Structural basis of drug resistance for the V82A mutant of HIV-1 proteinase," *Nat. Struct. Biol.* 2(3):244-9 (1995).

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### Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,



Robert A. Hodges  
Reg. No. 41,074

Dated: July 25, 2000

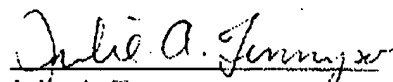
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I hereby certify that this Information Disclosure Statement, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

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Julie A. Tennyson

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		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
		Group Art Unit	1614
		Examiner Name	
Sheet	1	of	6
		Attorney Docket Number	OMRF 176

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.†	Included name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	1*
		BAI DWIN, et al., "Structural basis of drug resistance for the V82A mutant of HIV-1 proteinase," <i>Nat. Struct. Biol.</i> 2(13):244-9 (1995).	
		BOGER, "Renin Inhibitors. Design of Angiotensinogen Transition-state Analogs Containing Statine: Conformationally restricted inhibitors and a model for the bound conformation of renin substrate," in <i>Aspartic Proteinases and Their Inhibitors</i> , (Kostka, V., ed.), pp. 401-420, Walter de Gruyter: N.Y., 1985.	
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		CARROLL, et al., "Identification of potent inhibitors of <i>Plasmodium falciparum</i> plasmepsin II from an encoded statine combinatorial library," <i>Bioorg. Med. Chem. Lett.</i> 8(17):2315-20 (1998).	
		CARROLL, et al., "Evaluation of a structure based statine cyclic di-amino amide encoded combinatorial library against plasmepsin II and cathepsin D," <i>Bioorg. Med. Chem. Lett.</i> 8(22):3203-6 (1998).	
		CHEN, et al., "Three-dimensional structure of a mutant HIV-1 protease displaying cross-resistance to all protease inhibitors in clinical trials," <i>J. Biol. Chem.</i> 270(37):21433-6 (1995).	
		COFFIN, "HIV population dynamics in vivo: implications for genetic variation, pathogenesis, and therapy," <i>Science</i> 267(5197):483-9 (1995).	
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		CONDRA, et al., "In vivo emergence of HIV 1 variants resistant to multiple protease inhibitors," <i>Nature</i> 374(6522):569-71 (1995).	
		CRAIG, et al., "Antiviral properties of Ro 31-8959, an inhibitor of human immunodeficiency virus (HIV) proteinase," <i>Antiviral Res.</i> 16(4):295-305 (1991).	

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
		Group Art Unit	1614
		Examiner Name	
Sheet 2 of 6	Attorney Docket Number	OMRF 176	

OTHER ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume/issue number(s), publisher, city and/or country where published	1*
		DEBOUCK & METCALF, "Human immunodeficiency Virus Protease: A target for AIDS therapy," <i>Drug Devel. Res.</i> 21:1-17 (1990).	
		DEBOUCK, et al., "Human immunodeficiency virus protease expressed in <i>Escherichia coli</i> exhibits autoprocessing and specific maturation of the gag precursor," <i>Proc. Natl. Acad. Sci. USA</i> 84:8903-8907 (1987).	
		DORSEY, et al., "1-735,524: the design of a potent and orally bioavailable HIV protease inhibitor," <i>J. Med. Chem.</i> 37(21):3443-51 (1994).	
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		ERMOLIEFF, et al., "Kinetic properties of equine immunodeficiency virus type 1 protease and their implications in drug resistance <i>in Vivo</i> ," <i>Biochemistry</i> 36(40):12364-70 (1997).	
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Examiner's Signature	Date Considered
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<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16.4, if possible. <sup>6</sup> Applicant to place a check mark here if English language translation is attached.

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		First Named Inventor	Jordan J.N. Tang
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		Attorney Docket Number	OMRF 176
Sheet	3	of	6

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
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		HONG, et al., "Active-site mobility in human immunodeficiency virus, type 1, protease as demonstrated by crystal structure of A285 mutant." <i>Protein Sci.</i> 7(2):300-5 (1998).	
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		IDO, et al., "Kinetic studies of human immunodeficiency virus type 1 protease and its active-site hydrogen bond mutant A28S." <i>J. Biol. Chem.</i> 266(36):24359-66 (1991).	
		JACOBSEN, et al., "Characterization of human immunodeficiency virus type 1 mutants with decreased sensitivity to proteinase inhibitor Ro 31-8959." <i>Virology</i> 206(1):527-34 (1995).	
		JACOBSEN, et al., "In vivo resistance to a human immunodeficiency virus type 1 proteinase inhibitor: mutations, kinetics, and frequencies." <i>J. Infect. Dis.</i> 173(6):1379-87 (1996).	
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		LIN, et al., "Effect of point mutations on the kinetics and the inhibition of human immunodeficiency type 1 protease: Relationship to drug resistance," <i>Biochemistry</i> 34:1143-1152 (1995).	
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		Filing Date	February 18, 2000
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		RIDKY & LEIS, "Development of drug resistance to HIV-1 protease inhibitors," <i>J. Biol. Chem.</i> 270(50):29621-3 (1995).	
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		TOMASSELLI, et al., "The complexities of AIDS: An assessment of the HIV protease as a therapeutic target," <i>Chimicaoggi Chemistry Today</i> 9:6-27 (1991).	

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		Application Number	09/506,988
Sheet	6	of	6
		Filing Date	February 18, 2000
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		TONG, et al., "Crystal structure of human immunodeficiency virus (HIV) type 2 protease in complex with a reduced amide inhibitor and comparison with HIV-1 protease structures," <i>Proc. Natl. Acad. Sci. USA</i> 90(18):8387-91 (1993).	
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		WLODAWER, et al., "Conserved folding in retroviral proteases: crystal structure of a synthetic HIV-1 protease," <i>Science</i> 245(4918):616-21 (1989).	

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